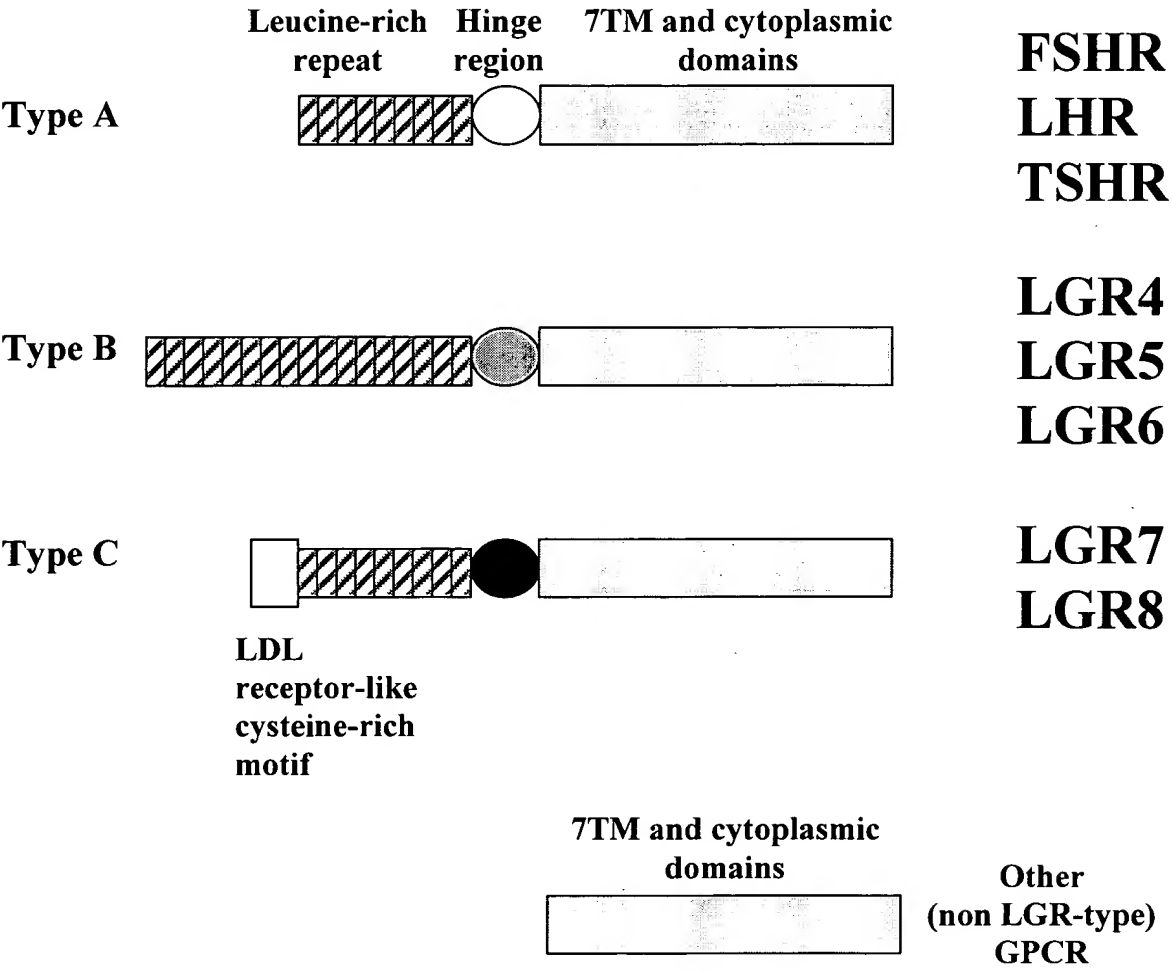




09/647,067
Exhibit 1

Schematic representation of functional domains in LGR family receptors



09/647,067

Exhibit 2

Alignment of LGR7 with LH receptor

Identities = 148/636 (23%), Positives = 289/636 (45%)

```
LGR7 : 89 EAETPECLVGSVPVQCCLCQGLELDCDETNLRAVPSVSSNVTAMSLQWNLIRKLPPDCFKN 148
      EA PE      P C+ G L C      P ++ +T +SL + ++ +P F+
LHR : 27 EALCPE-----PCNCVPDGA-LRC-----PGPTAGLTRLSLAYLPVKVIPSQAFRG 71

LGR7 : 149 YHDLQKLYL-QNNKITSISIIYAFRGLNSLTKLYLSHNR-ITFLKPGVFEDLHRLEWLIIE 206
      +++ K+ + Q + + I AF L +L+++ + + + + +++PG F +L L++L I
LHR : 72 LNEVIKIEISQIDSLERIEANAFDNLLNLSEILIQNTKNLRYIEPGAFINLPLGLKLYLSIC 131

LGR7 : 207 DNHLRSRISPPT--FYGLNSLILLVLMNNVLTSLPDKPLCQHMPRLHWLDLEGNHIHNLRN 264
      + + + T F ++ IL + N +T +P      L L GN +++ -
LHR : 132 NTGIRKFPDVTKVFSSESFILEICDNLHITTPGNAFQGMNNEVTLKLYGNGFEEVQS 191

LGR7 : 265 LTFISCSNLTVLVMRKN-KINHLNENTFAPLQKLDLDELGLSNKIEENLPPLIFKDLKEL-- 321
      F + + LT L +++N + ++ F      LD+ S K++ LP + ++ L
LHR : 192 HAF-NGTTLSLELKENVHLEKMHNGAFRGATGPKTLDISSTKLQALPSYGLESIQRLIA 250

LGR7 : 322 -SQLNLSYNPIQKIQANQFD-----YLVKLKSLSLLEGIEISNI----- 358
      S +L P ++ N +      + ++L + S+
LHR : 251 TSSYSLKKLPSRETFFVNLEATLTYPSSHCAFRNLPTKEQNFSHSISENFSKQCESTVRK 310

LGR7 : 359 --QORMFRPLMNLSHIYFKKFQYCGYAPHVRSCKPNTDGISSLENLLASIIQRVFVWVVS 416
      + ++ ++ S + ++Y P C P D + E+++ RV +W+++
LHR : 311 VSNKTLYSMLAESELSGWDYEYGFCLPKTPRCAPEPDAPNCPEDIMGYDFLRVLIWLIN 370

LGR7 : 417 AVTCFGNIFVICMRPYIRSENKLYAMSIISLCCADCLMGIYLFVIGGFDLKRGEYNKHA 476
      + GN+ V+ + R + + + +L AD MG+YL +I D + +G+Y HA
LHR : 371 ILAIMGNMTVLVLLTSRYKLTVPFRFLMCNLSFADFCMGLYLLLIASVDSQTKGQYYNHA 430

LGR7 : 477 QLWMESTHCQLVGSLAILSTEVSVLLLTFLTLEKYICIVYPFRVPRPGKCR-TITVLILI 535
      W + C G + ++E+SV LT +TLE++ I Y + + R I +++
LHR : 431 IDWQTGSGCSTAGFFTTFASELSVYTLTVITLERWHTITYAIHLDQKLRLRHAILIMLGG 490

LGR7 : 536 WITGFIVAFIPLSNKEFFKNYYGTNGVCFPLHSEDTESIGAQIYSVAIFLGINLAAFIIE 595
      W+ ++A +PL NY + +CFP+ D E+ +Q+Y + I + +N+ AF II
LHR : 491 WLFSSLIAMLPVVG---VSNYMKVS-ICFPM---DVETTLNQVYILTILI-LNVVAFFII 542

LGR7 : 596 VFSYGSFMFYSHQSAITATEIRNQVKEMILAKRFFIFVFTDALCWIPIFVVKFSLSLQV 655
      Y ++++V + AT K+ +AK+ ++FTD C PI + +V
LHR : 543 CACYIKIYFAVRNPELMAT-----NKDTKIAKKMAILIFTDFTCMAPISFFAISAAFKV 596

LGR7 : 656 EIPGTITSWVIFIL--PINSALNPILYTLTTRPFK 689
      + T+T+ V+ +L PINS NP LY + T+ F+
LHR : 597 PLI-TVTNSKVLLVLFYPINSCANPFLYAIFTKTFTQ 631
```

09/647,067
Exhibit 3

Alignment of LGR7 with TSH receptor

```

LGR7 : 106 LPPDCFKNY-HDLQKLDLQNNKITSISIIYAFRGLNSLTkLYLSHNR-ITFLKPGVFEDLH 163
      +P + F+  ++  L L NN TS+ YAF G  L +YL+ N+ +T +  F  ++
TSHR : 167 IPVNAFQGLCNETLTkLYNNGFTSVQGYAFNG-TKLDAYLNKNKYLTVIDKDAFGGVY 225

LGR7 : 164 RLEWLIIEDNHLSRISPPTFYGLNSLILLVLMNN-VLTRLDPKPLCQHMPRLHWLDLE-G 221
      L+ D  + ++  GL L L+ N  L +LP  H+ R  DL
TSHR : 226 SGPSLL--DVSQTSVTALPSKGLEHLKELIARNTWTLKKLPLSLSFLHLTRA---DLSYP 280

LGR7 : 222 NHIHNLRN-----LTFISCSNLTVLVMRKNK-INHLNENTFAPLQKLDLGLGSKNIE 273
      +H  +N      L  + C+ ++  +R+ K +N LN  +PL +  E +LG + +
TSHR : 281 SHCCAFKNQKKIRGILESMLCNESSMQSLRQRKSVNALN----SPLHQEYEENLGDSIV- 335

LGR7 : 274 NLPPLIFKDLKELSQLNLSYNPIQKIQANQFDYLVKLSLSLEGIEISNIQORMFRPLMN 333
      KE S+  ++N      A+ + + + +  EI  Q + P
TSHR : 336 -----GYKEKSKFQDTHN-----NAHYVVFEEQED-----EIIGFGQELKNPQEE 376

                                     → TM1

LGR7 : 334 LSHIYFKKFQY--CGYAPHVRSCKPNTDGISSLENLLASIIQRVFWVVS AVTCFGNIFV 391
      +  + Y  CG +  +  C P +D +  E+++  R+ VW VS +  GN+ FV
TSHR : 377 TLQAFDSHYDYTCGDSEDM-VCTPKSDEFNPCEDIMGYKFLRIVVWFVSLALLGNV FV 435

LGR7 : 392 ICMRPYIRSENKLYAMSIISLCCADCLMGIYLFVIGGFDLKFGEYNKHAQLWMESTHCQ 451
      + +  +  +  + +L AD MG+YL +I  DL  EY HA W  C
TSHR : 436 LLILLTSHYKLNVPFLMCNLAFADFCMGMYLLLIASVDLYTHSEYYNHAI DWQTGPGCN 495

LGR7 : 452 LVGSLAILSTEVSVLLLFTLTLEKYICIVYPRFCVRPGKCR-TITVLILIWITGFIVAFI 510
      G  + ++E+SV LT +TLE++ I +  R R + R  +++ W+ F++A +
TSHR : 496 TAGFFT VFASELSVYTLTVITLERWYAITFAMRLDRKIRLRHACAIMVG GWVCCFLLALL 555

LGR7 : 511 PLSNKEFFKNYYGTNGVCFPLHSEDTESIGAQIYSVAIFLGINLAAFI IIVFSYGS MFYS 570
      PL  + Y  +C P+  DTE+  A Y V + L +N+ AF+I+  +  ++ +
TSHR : 556 PLVG----ISSYAKVSICLPM---DTETPLALAYIVFV-LTLNIVAFVIVCCCHVKIYIT 607

LGR7 : 571 VHQS AITATEIRNQVKKEMILAKRFFFIVFTDALCWIPIFVVKFSL LQVEIPGTITSWV 630
      V      N  K+  +AKR  ++FTD +C PI  ++L  +  T+++
TSHR : 608 VRNPQY-----NPGDKDTKIAKRM AVLIFTDFICMAPISFYALSAILNKPLI-TVSN SK 660

LGR7 : 631 VIFIL--PINSALNPILYTLTTRPFKE----MIHRFWYNYRQRKSMD SKGQKTYAHHSSG 684
      ++ +L P+NS NP LY + T+ F+  ++ +F  RQ ++  +GQ+  +S+
TSHR : 661 ILLVLFYPLNSCANPFLYAIFTKAFQRDV FILLSKFGICKRQAQAY--RGQRVPPKNSTD 718

LGR7 : 685 VEM 687
      +++
TSHR : 719 IQV 721

```

09/647,067

Exhibit 4

SEQUENCE ALIGNMENT OF HUMAN LGR7, LGR8, AND TSHR.

LGR8: MIVFLVFKHLFSLRLITMFFLLHFIVLINVKDFALT 36
LGR7: MTSGSVFFYILIFGKYFSHGGG 22

LGR8: 37 QGSMITPSQKGYFPCGNLTKCLERAFHCDKDDCGNGADENCGDTSWATIEGTVHGNANSV----- 100
LGR7: 23 ----QDVKSLGYFPCGNITKCLHQLLHCNIVDDCGNQADEDNCGDNNGWSMQEDKYFASYKMTSQYPF 88

→ LRR1 → LRR2

LGR8: 101 -ALLIQEFLKQYEQCCDCKETEIEGVNGDKSVEMISNNVILLSTKKNKTHSEEDKVEIKYTKKKIFLC 169
LGR7: 89 EAETPECLVGSVEVOGLCQGLEIDDETNRRAVHSVSSNVVTAMSLQWNLHRKEPDCEKNNHDLQKLYLC 158
TSHR IEVNAEQGLCNETLTCLK

→ LRR3 → LRR4 → LRR5

LGR8: 170 HNCIRHTSRKAFFGICNLQILYINHC-LITLREGIEKDLHOTWLLLDNPITRISQRLTSLNSLFFIS 239
LGR7: 159 NNKITTSISIAERGLNSITKLYISHNR-LITFKPGVEEDLHREWLLIEDNHLSTRISPPTEYGLNSIILLV 228
TSHR YNNGFTSVQGYAFNGTK-LDAVYLNKNKYLLVIDKDAFGGVYSGPSLL--DVSQTSVTALPSKGLIEHLKEIIA

→ LRR6 → LRR7 → LRR8

LGR8: 240 MVNNYIEALF-KOMCAQMFQINAVDLEGNRKRYTNSSTFLSCDSLTVILFPRNQTGFVPEKTESS-LKN-IG 308
LGR7: 229 LMNNVITRELDKPLCOHMERLHLDOLEGNHNNRNLLLETSCSNLTIVVMRKNNKINHLNENDEAP-LQK-ID 298
TSHR RNTWTLKKLELSLSFLHLTA---DLSYPSCCAFKNQKKIRGILESLMCNESSMQSLRQRKSVNALNSPI

→ LRR9 → LRR10

LGR8: 309 ELDISNTTETSEHLKDLKLLQKINLSSNMLYLHKNOESTKOTOSTDERETPNNTRMEOEMKN 378
LGR7: 299 ELDIGSNKLENIPELIEKDLKELISQNLSSYNIQKIQANQETIVVKLSISLEGIEISNIOQEMERELMN 368
TSHR HQYEENLGDSIV--GYKESKEFDTHNNAHYVFEE---QED-----IIGFQQLKNPQEETLQAF--

→ TM1 → IL1

LGR8: 379 LSHIYKNNRYCYAPHVRIOMELTDGSISSFDDLIANNILRIEIVWMAFIICFCNLFVIGMRSFTKAENT 448
LGR7: 369 LSHIYENKEQYCGYAPHVRSCKENTDGISSLENLLASITQSVFVWVVSAVICFCNIEVTCMRPYRSENK 438
TSHR DSH-M--DYTICGDSMD-VGTEKSEDFNPCEIDIMGYKFLSIVVWFVSLALLGNVEVLLILLTSHYKLN

→ TM2 → EL1 → TM3

LGR8: 449 THAMSTKILCCADCLMGVYLFVCIFFDIYRGOYQYALLWMESVQRMCFEFLAMESTEVSVLLTYLTI 518
LGR7: 439 LYAMSTIISLCCADCLMGVYLFVIGGEDLRFGEYNNKHAQLWMESTHQLVGSLLAILSTEVSVLLTFLTI 508
TSHR PRFLMCNLAFADF-C-MGMVILLIASVDLYTHSEYNNHAIDHQTGPGONTAGFFTTFASLSMYTLTVITI

→ IL2 → TM4 → EL2 → TM5

LGR8: 519 EKFLVIVFPESNIRPGKROISVILTCIMAGSLIAVIEFWNKDYEGNFYKNGVFPYIYDQEDIGSKG 588
LGR7: 509 EKYICIVYPERCVRPCKCRITVLLILWITSHIVAFIPLSNKEFEKNNYGTNGVFPYHSEDTESIGAQI 578
TSHR ERWYAITFAMRDRKIRLRHACAIMVGGVCCCELLALLPIVG---ISSMAKVSICLEM---DTETPLALA

→ IL3 → TM6

LGR8: 589 YSLGIFLGVNLLAFLIVFSYITMECSIQKTALOTTEVERNCFGRVAVANRFEFFIVSDATCWIEFVVK 658
LGR7: 579 YSVATFLGINLAAGIILVESYSGMEYSVHQSITATEIRNOVKKEMILAKREFFIVFTDALCWIPFVVK 648
TSHR MIVFV-LTLNIVAEVIVCCCHVKIYITMRNPQY-----NPGDKDTKIARMAVLIETLFCMAPIISFYA

09/647,067

Exhibit 4

→ EL3 → TM7

LGR8: 659 ILSIFRVEEDIMTSWIVHFLFVNSALNPILYILTNFEDKLKQHH-ORKSIFKI--KKSLSTSIV 727

LGR7: 649 FLSILOVELEGHISVVIHLEINSALNPILYILTRPEKEMIHRFWYNYRORKSMSDK--GKTYAPFI 718

TSHR LSAILNKPLITVSNKILLLE-YELNSCANFLYALFTKAFQRDVFILSKFGICKRQAQAYRCORVPPKNST

LGR8: 729 IISDSSSLKLGVLNKITLGDSIMKPVS* 755

LGR7: 719 VVEMWPLQEMPPELMKPDLFYPCEMSLISQSTRLNSYS* 757

TSHR DIQV



RECEIVED
OCT 29 2003
TECH CENTER 1600/2900

5/8

>Alignment of LGR7-L with LGR7-S
Query=LGR7-L
Sbjct=LGR7-S

```
Query: 1  MTSGSVFFYILIFGKYFSHGGGQDVKCSLGYFPCGNITKCLPQLLHCNGVDDCGNQADE 60
          MTSGSVFFYILIFGKYFSHGGGQDVKCSLGYFPCGNITKCLPQLLHCNGVDDCGNQADE
Sbjct: 1  MTSGSVFFYILIFGKYFSHGGGQDVKCSLGYFPCGNITKCLPQLLHCNGVDDCGNQADE 60

Query: 61  NCGDNNGWSMQFDKYFASYKMTSQYPFEAETPECLVGSVPVQCLCQ---GLELDCDETN 117
          NC                               V V C C   GLELD +
Sbjct: 61  NC-----VVVLCQCMSLPGLELDWMKP- 82

Query: 118  LRAVPSVSSNVTAMSLQWNLIRKLPPDCFKNYHDLQKLYLQNNKITSISIIYAFRGLNSLT 177
          +VPSVSSNVTAMSLQWNLIRKLPPDCFKNYHDLQKL LQNNKITSISIIYAFRGLNSLT
Sbjct: 83  FTSVPSVSSNVTAMSLQWNLIRKLPPDCFKNYHDLQKLDLQNNKITSISIIYAFRGLNSLT 142

Query: 178  KLYLSHNRIITFLKPGVFEDLHRLEWLIIEDNHLSRISPPTFYGLNSLILLVLMNNVLTRL 237
          KLYLSHNRIITFLKPGVFEDLHRLEWLIIEDNHLSRISPPTFYGLNSLILLVLMNNVLTRL
Sbjct: 143 KLYLSHNRIITFLKPGVFEDLHRLEWLIIEDNHLSRISPPTFYGLNSLILLVLMNNVLTRL 202

Query: 238  PDKPLCQHMPRLHWDLEGNHIHNLRLNLTIFISCSNLTVLVMRKNKINHLNENTFAPLQKL 297
          PDKPLCQHMPRLHWDLEGNHIHNLRLNLTIFISCSNLTVLVMRKNKINHLNENTFAPLQKL
Sbjct: 203 PDKPLCQHMPRLHWDLEGNHIHNLRLNLTIFISCSNLTVLVMRKNKINHLNENTFAPLQKL 262

Query: 298  DELDLGSNKIENLPPLIFKDLKELSQNLNSYNPIQKIQANQFDYLVKLKSLSLLEGIEISN 357
          DELDLGSNKIENLPPLIFKDLKELSQNLNSYNPIQKIQANQFDYLVKLKSLSLLEGIEISN
Sbjct: 263 DELDLGSNKIENLPPLIFKDLKELSQNLNSYNPIQKIQANQFDYLVKLKSLSLLEGIEISN 322

Query: 358  IQQRMFRPLMNLSHIYFKKFQYCGYAPHVRSCPNITDGISSLENLLASIIQRFVFWVWSA 417
          IQQRMFRPLMNLSHIYFKKFQYCGYAPHVRSCPNITDGISSLENLLASIIQRFVFWVWSA
Sbjct: 323 IQQRMFRPLMNLSHIYFKKFQYCGYAPHVRSCPNITDGISSLENLLASIIQRFVFWVWSA 382

Query: 418  VTCFGNIFVICMRPYIRSENKLYAMSIIISLCCADCLMGIYLFVIGGFDLKFRGEYNKHAQ 477
          VTCFGNIFVICMRPYIRSENKLYAMSIIISLCCADCLMGIYLFVIGGFDLKFRGEYNKHAQ
Sbjct: 383 VTCFGNIFVICMRPYIRSENKLYAMSIIISLCCADCLMGIYLFVIGGFDLKFRGEYNKHAQ 442

Query: 478  LWMESTHCQLVGSLAILSTEVSLLLLTFLTLEKYICIVYPFRCVRPKGKCRITITVLILIWI 537
          LWMESTHCQLVGSLAILSTEVSLLLLTFLTLEKYICIVYPFRCVRPKGKCRITITVLILIWI
Sbjct: 443 LWMESTHCQLVGSLAILSTEVSLLLLTFLTLEKYICIVYPFRCVRPKGKCRITITVLILIWI 502

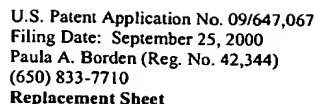
Query: 538  TGFIVAFIPLSNKEFFKNYYGTNGVCFPLHSEDTE SIGAQIYSVAIFLGINLAAFIIIVF 597
          TGFIVAFIPLSNKEFFKNYYGTNGVCFPLHSEDTE SIGAQIYSVAIFLGINLAAFIIIVF
Sbjct: 503 TGFIVAFIPLSNKEFFKNYYGTNGVCFPLHSEDTE SIGAQIYSVAIFLGINLAAFIIIVF 562

Query: 598  SYGSMFYSVHQSAITATEIRNQVKKEMILAKRFFFIVFTDALCWIPFVVKFLSLLQVEI 657
          SYGSMFYSVHQSAITATEIRNQVKKEMILAKRFFFIVFTDALCWIPFVVKFLSLLQVEI
Sbjct: 563 SYGSMFYSVHQSAITATEIRNQVKKEMILAKRFFFIVFTDALCWIPFVVKFLSLLQVEI 622

Query: 658  PGTITSWVVIFILPINSALNPILYTLTTRPFKEMIHRFWYNYRQRKSMSDKGQKTYAPSF 717
          PGTITSWVVIFILPINSALNPILYTLTTRPFKEMIHRFWYNYRQRKSMSDKGQKTYAPSF
Sbjct: 623 PGTITSWVVIFILPINSALNPILYTLTTRPFKEMIHRFWYNYRQRKSMSDKGQKTYAPSF 682

Query: 718  IWVEMWPLQEMPPELMKPDLTYPCEMSLISQSTRLNSYS 757 (SEQ ID NO:06)
          IWVEMWPLQEMPPELMKPDLTYPCEMSLISQSTRLNSYS (SEQ ID NO:09)
Sbjct: 683 IWVEMWPLQEMPPELMKPDLTYPCEMSLISQSTRLNSYS 722 (SEQ ID NO:08)
```

FIG. 5



OCT 29 2003

TECH CENTER 1600/2900

6/8

Signal peptide

LGR4 MPGPLGLLLCFLALGLLGSAGPSGA (SEQ ID NO:10)
LGR5 MDTSR LGVLLSLPVLQLATG (SEQ ID NO:11)
LHR MKQRFSA LQLKLLLLLPPLPRA (SEQ ID NO:12)
FSHR MALLLVSLAFLSLGSG (SEQ ID NO:13)
TSHR MRPADLLQLVLLLDLPDLGG (SEQ ID NO:14)

N-flank cysteine-rich sequence

LGR4	APPL	AA-P	S	DGDR---	RVD	SGKGLTAVPEGLSAFTQA	(SEQ ID NO:15)
LGR5	GSSPRSGVLLRG	P-TH	H	EPDGRMLLRVD		SDLGLSELPSNLSVFTSY	(SEQ ID NO:16)
LHR	LREAL	P-EP	N	VPDG--	ALR--	PGPTAGLTR	(SEQ ID NO:17)
FSHR		HHRI	H	SNRVFL----		QESKVTEIPSDLPRNAIE	(SEQ ID NO:18)
TSHR	MG	SSPP	E	HQVED--	FRVT	KDIQRIPSLPPSTQT	(SEQ ID NO:19)

Leucine-rich repeats

LGR4	DISMNNITQLPED	KSFPFLEELQLAGN	--	SL	HPKALSG	KE	KVLTQ	--	Q
LGR5	DLSMNNISQLLPNPLPSLHFLLEELRLAGNA--	TY	PKGA	TG	YS	KVLMQ	--	Q	
LHR	SLAYLPVKVIPSQ	RLNVEVIKIEISQI	S-	ER	EANA	DN	LN	SEIIQ	TK -
FSHR	RFLVTLKLRVIOQG	SGFGLEKIEISQN	V-	EV	EADV	SN	PK	HEIRIEKAN	-
TSHR	KLIETHLRTIPSH	SNLPNISRIYVSI-	VT	QQLES	SHS	YN	SKVTHIEIR	TR	-

LGR4	RTV-	SE	IHG	SA	QS	RLDA	H-	TSV	EDS--	FEGVLQLRH	WLD	S-L-	EV	VR
LGR5	RHV-	TE	LQN	RS	QS	RLDA	H-	SYV	P-SC-	FSGLHSLRH	WLD	A-L-	E	VQ
LHR	RYIE	-G	FIN	PG	KY	SIC-	TG	RKF	DVTKVFSSES	ENFI	EIC	LHI-	T	GN
FSHR	LYIN	-E	FQN	PN	QY	LIS-	TG	KHL	DVHK-	IHSLOKVL-	DIQ	INIH	-	ERN
TSHR	TYID	-D	LKE	PL	KF	GIF-	TGLKMF	DLTK-	VYSTD	DIFFI	EIT	PYM-	S	VN

LGR4	PLSN	P-TLQA	T	AL	NISSIPDF	T	LSS	VV	H	HN	K-IKSLSQHC	D	LDN-LE	
LGR5	A	RS	S-ALQAMT	AL	KIHHPDY	G	LSSVVV	H	HN	R-IHSLGKCC	D	LHS-LE		
LHR	A	QGMN	SVT	K	YG	GFEVQSH	-	GTT	TS	E	KE	VHLEKMHGA	R	A-TGPK
FSHR	S	VG	SFESVI	W	NK	GIQEIHNC	-	GTO	DE	N	SD	NLEELPNDV	H	A-SGPV
TSHR	A	QG	CNETLT	K	YN	GFTSVQGY	-	GTK	DAVY	NK	KYLTVIDKDA	G	VYSGPS	

```

LGR4  T  LNYNYLDEF Q-AIKA PS  KELGFHSNSISVI D-GA GGNPL RTIH - DNPLS
LGR5  T  LNYNNLDEF T-AIRT SN  KELGFHSNNIRSI E-KA VGNP S ITIHF- DNPIQ
LHR   T  ISSTKLQAL SYGLESIQ R I-ATS-SYSLKKL SRET V-N--- LEAT T  ----(SEQ ID NO:22)
FSHR  I  ISRTRHSL  SYGLEN KK  R-ARSTYN-LKKL TLEKLVA--- MEAS T  ----(SEQ ID NO:23)
TSHR  L  VSOTSVAL  SKGLEH KE  I-ARNTWT-LKKL LSL S LH---  TRAD S  ----(SEQ ID NO:24)

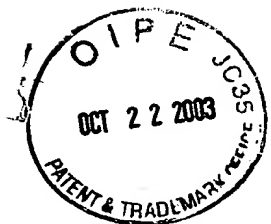
```

```

LGR4      FVGNSAFHNLSDLHCLVIRGASLVQWFFNLTGTVHLESITLTGTKISSIPDDLQCNQKML
LGR5      FVGRSAFOHLPELRTLTLNGASQITEFPDLTG TANLESITLTGAQISSLPQTVCNQLPNL
LHR       -----
FSHR      -----
TSHR      -----

```

FIG. 6A



RECEIVED
OCT 29 2003
TECH CENTER 1600/2900

7/8

RTLDLSYNNIRDLPSPNGCRAL E E I S L Q R N Q I S L I K E N T F Q G L T S L R I L D L S R N L I R E I H
QVLDLSYNLLEDLPSPFVCQKLQKIDLRHNEIYEIKVDTFQQLLSLRLSLNLAWNKAIIH

SGAFAKLGTITNLDVSFNELTSFPTEGLNGLNQLK (SEQ ID NO:20)
PNAFSTLP SLIKL DLSSNLLSSFPITGLHGLTHLK (SEQ ID NO:21)

C-flank cysteine-rich sequence

LGR4	LVGNFKLKDALAARDFANLRSLSV	YAYQ	WGCDSLCKLNTEDNSPQEHSVTKEGA
LGR5	LTGNHALQSLISSENFPELVKVIEM	YAYQ	GVCENAYKISNQWNKGDNSMDDLHKK
LHR	-----	--SH	RNLPTKEQNFSHSISENFSKQCESTVR
FSHR	-----	--SH	ANWRRQISELHPICNKSILRQEVDMYT
TSHR	-----	--SH	KNQKKIRGILESIMCNESMQLRQRK

LGR4	TDAANVTSTAENE	HS	-----
LGR5	DAGMFQAQDERDL	DF	-----
LHR	KVSNKTYSSMLA	SE	-----
FSHR	QTRGQRSSLAEDN	SS	-----
TSHR	SVNALNSPLHQEY	ENLGDSIVGYKEKSKFQDTHNNAHYVFFEEQEDEIIIGFGQELKNP	

LGR4	-----QIIH	T	STGA	K	YLLGSWMI	(SEQ ID NO:25)
LGR5	-----LLDFEEDLKALHSVQ	S	SPGP	K	HLLDGWLI	(SEQ ID NO:26)
LHR	-----LSGWDYEGFCLPKTPR	-	A	EPDA	N	DIMGYDFL (SEQ ID NO:27)
FSHR	YSRGFDMTYTEFDYDLCEVVDVT	S	KPDA	N	DIMGYNIL	(SEQ ID NO:28)
TSHR	QEETLQAFDSDHYDTICGDSSEDMV	T	KSDE	N	DIMGYKFL	(SEQ ID NO:29)

Transmembrane

	TM 1										TM 2									
LGR4	LTV	F	FLV	LLF	LL	ILTVFA	CSS	PASKL	FIGLISVSNLLM	IYTGILTF	L	AVSW								
LGR5	IGV	T	AV	LTC	AL	TSTVFR	PLYISPIKL	IGVIAAVNMLT	VSSAVL	G	AF	F								
LHR	VLI	L	NI	IMG	MT	LFVLLT	RYK	TVPRF	MCNLSFADFCM	LYLLLI	S	SQ	K							
FSHR	VLI	F	SI	ITG	II	LVILTT	QYK	TVPRF	MCNLAFADLCI	IYLLLI	S	IH	K							
TSHR	IVV	FVSL	LLG	VF	LLILLT	HYK	NVPRF	MCNLAFADFCM	MYLLLI	S	LY	H								

	TM 3												
LGR4	GRFAEFG	W	E	S	KV	SLA	S	SA	FL	LAAV	SVFAKDLMKHGKSSH	QF	
LGR5	GSFARHGAW	EN	V	HVI	LSI			S	FL	LAA	GFSVKYSAKFET	APFSSL	
LHR	GQYYNHA	D	Q	S	ST	FT		L	YT	VIT	WHTITYAIHLDO	LR	HA
FSHR	SQYHNHA	D	Q	A	DA	FT		L	YT	AIT	WHTITHAMQLDC	VQ	HA
TSHR	SEYYNHA	D	Q	P	NT	FT		L	YT	VIT	WYAITFAMRLDR	IR	HA

FIG. 6B



RECEIVED
OCT 29 2003
TECH CENTER 1600/2900

TM 4					TM 5				
LGR4	QVAALLALLGAAVAGCF	FHGGQ	SASPL	FPTGETPSLGFTVTLVL	SL	LLMA			
LGR5	KVIILLCALLALTM AV	L G K	GASPL	LPFGEPSTMG MVALIL	SLC	LMMT			
LHR	ILIMLGGLFSSLI ML	V V N	MKVSIF	MDVETTL SQV ILTILI	VV	FIIC			
FSHR	ASVMVMGWIFAFAA LF	IF I S	MKVSIF	MDIDSPLSQL VMSLLV	VL	VVIC			
TSHR	CAIMVGWVCCFLL LL	V I S	AKVSI	MDTETPLALA IVFVLT	IV	VIVC			
TM 6									
LGR4	II T L	CNL-EKEDLSENSQSSVI	HV W	NCIFFC	VA	PSFAPLITAIS	SPEI		
LGR5	IA T L	CNL-DKGDLENIW CSMV	HI L L	NCILNC	VA	LSF SLINLTF	SPEV		
LHR	AC I I	FAVRNPELMATNK TKIA	KM I	DFTCMA	IS	FAI AAFKVPL	TVTN		
FSHR	GC IHI	LTVRNPNI VSSSS	TRIA RM M	DFLCMA	IS	FAI ASLKVPL	TVSK		
TSHR	CCHV I	ITVRNPQYNPGDK TKIA	RM V	DFICMA	IS	YAL AILNKPL	TVSN		
TM 7									
LGR4	M SVTLI	F LPA L	V VF N	(SEQ ID NO:30)					
LGR5	I FI LVVV	LPA L L	IL N	(SEQ ID NO:31)					
LHR	S VL VL	Y INS A	F AI T	(SEQ ID NO:32)					
FSHR	A IL VL	H INS A	F AI T	(SEQ ID NO:33)					
TSHR	S IL VL	Y LNS A	F AI T	(SEQ ID NO:34)					
C-terminal tail									
LGR4	PK KE WKL	KRRVTRKHGSVSVS	ISSQGGCGEQDFYYDCGMYSHLQGNLTVCDCCESFL						
LGR5	PH KE LVS	RKQTYVWTRSKHPSLMS	INSDDVEKQSCDSTQALVTFTSSSITYDLPPSS						
LHR	KT QR FFL	LSKFGCCRRRAELYRRKDF	SAYTSNCKNGFTGSNKPSQSTLKLSTLHCQG						
FSHR	KN RR FFI	LSKCGCYEMQAQIYRTETS	STVHNTHPRNGHCSSAPRV TNGSTYILVPLS						
TSHR	KA QR VFI	LSKFGICKRQAQAYRGQR	VPPKNSTDIQVQKVTHDMRQGLHNMEDVYELI						
LGR4	LTKPVSC	KHLIKSHS	CPVLTAASCORPEAYWSDCGTQSAHSDYADEEDSFVSDSSDQVQA						
LGR5	VPSPAYF	VTESCHLSS	VAFVPCL (SEQ ID NO:36)						
LHR	TALLDK	TRYTEC	(SEQ ID NO:37)						
FSHR	HLAQN		(SEQ ID NO:38)						
TSHR	ENSHLTP	KKQGQISEEYMQTVL	(SEQ ID NO:39)						
LGR4	CGRACFY	QSRGFPLVRYAYNLQR	VRD (SEQ ID NO:35)						

FIG. 6C